

Claims

(59)

1. A method for producing mononuclear cells overexpressing IL-10, wherein the method comprises the steps of:
 - (a) providing a composition comprising peripheral blood mononuclear cells (from a mammal);
 - (b) introducing an expression construct comprising a nucleotide sequence encoding a polypeptide having IL-10 activity into at least part of the mononuclear cells; and,
 - (c) recovery of mononuclear cells overexpressing the polypeptide having IL-10 activity, wherein the mononuclear cells overexpressing the polypeptide having IL-10 activity are not specific for a predetermined antigen.
2. A method according to claim 1, wherein composition comprising peripheral blood mononuclear cells is enriched for a subfraction of the peripheral blood mononuclear cells.
3. A method according to claim 2, wherein the subfraction of mononuclear cells is selected from the group consisting of lymphocytes, B cells, T cells, CD4⁺ cells, macrophages, monocytes or dendritic cells (DC).
4. A method according to any one of claims 1 - 3, wherein prior to step (b) the mononuclear cells are proliferated.
5. A method according to claim 4, wherein the mononuclear cells are proliferated in the presence of a proliferating agent.
6. A method according to claim 5, wherein the proliferating agent is at least one of CD3/CD28 or PHA.
7. A method according any one of claim 1 - 6, wherein subsequent to (b) the mononuclear cells are enriched for a subfraction of mononuclear cells.
8. A method according to claim 7, wherein the subfraction of mononuclear cells is selected from the group consisting of lymphocytes, B cells, T cells, CD4⁺ cells, macrophages, monocytes or dendritic cells (DC).

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9. A method according to any one of claims 1 - 8, wherein subsequent to step (b) the mononuclear cells are enriched for cells (over)expressing the IL-10 transgene.
10. A method for producing a pharmaceutical composition comprising mononuclear cells overexpressing IL-10, mixing cells obtained in above claims with suitable pharmaceutical carrier.
11. A composition comprising mononuclear cells containing an IL-10 transgene, wherein the mononuclear cells are not specific for a predetermined antigen.
12. A composition according to claim 11, whereby the composition comprises T cells containing an IL-10 transgene.
13. A composition according to claim 12, whereby the T cells phenotypically mimic regulatory T cells in that the T cells decrease proliferation of autologous responder cells and/or decrease production of the pro-inflammatory cytokine IL-12 by dendritic cells.
14. A composition according to any one of claims 11 - 13, wherein the composition is a pharmaceutical composition comprising in addition to the mononuclear cells a pharmaceutically acceptable carrier.
15. A method of treating a disease associated with undesired activation and/or expansion of T cells, wherein the method comprises administering a pharmaceutical composition according to claim 14 to a subject suffering from a disease associated with undesired activation and/or expansion of T cells.
16. A method according to claim 15, wherein the disease associated with undesired activation and/or expansion of T cells is a Th1-mediated disease, more preferably Th1-mediated inflammatory diseases.
17. A method according to claim 16, wherein the Th1-mediated disease is selected from the group consisting of Crohn's disease, reactive arthritis, insulin-dependent diabetes, colitis, pancreatitis, an lung, an inflammatory eye disease, multiple sclerosis, Hashimoto's thyroiditis,

Grave's disease, chronic articular reumatism, contact dermatitis, psoriasis, graft rejection, graft versus host disease, and sarcoidosis.

18. A method according to any one of claims 15 - 17, wherein a the composition comprising the mononuclear cells is administered in a therapeutically effective amount.

19. Use of IL-10 overexpressing mononuclear cells as obtained by any of the methods of claims 1 - 9, in the manufacture of a medicament for use in the treatment of disease associated with undesired activation and/or expansion of T cells.